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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/598,854	05/15/2007	Douglas G. Johnson	0003.06/PCT-US	1320

25871 7590 05/25/2010

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EXAMINER
OH, TAYLOR V

ART UNIT	PAPER NUMBER
1625	

NOTIFICATION DATE	DELIVERY MODE
05/25/2010	ELECTRONIC

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Notice of the Office communication was sent electronically on above-indicated "Notification Date" to the following e-mail address(es):

efspatents@sbiplaw.com

Office Action Summary	Application No.	Applicant(s)	
	10/598,854	JOHNSON ET AL.	
	Examiner	Art Unit	
	Taylor Victor Oh	1625	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE *3* MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *04 May 2010*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-67* is/are pending in the application.

4a) Of the above claim(s) *42-51,53, and 67* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☐ Claim(s) *1-41,52 and 54-66* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☒ The drawing(s) filed on *13 September 2006* is/are: a)☒ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date *11/29/06*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

The Status of Claims:

Claims 1-67 are pending.

Claims 1-41,52, 54-59, and 60-66 are rejected.

DETAILED ACTION

1. Claims 1-41,52,54-59, and 60-66 are under consideration in this Office Action.

Priority

2. It is noted that this application is a 371 of PCT/US05/13709(04/22/2005), which claims benefit of 60/564,308(04/22/2004), claims benefit of 60/564,721(04/22/2004).

Drawings

3. The drawings filed on 9/13/06 are accepted by the examiner.

Election/Restriction

Applicant's election with traverse of Group I (claims 1-41,52,54-59, and 60-66) on 05/04/2010 is acknowledged.

Claims 42-51,53, and 67 are withdrawn from further consideration pursuant to 37 CFR 1.142(b) as being drawn to nonelected groups I-XI, there being no allowable generic or linking claim.

Claim Rejections - 35 USC § 102

2113 [R-1] Product-by-Process Claims

PRODUCT-BY-PROCESS CLAIMS ARE NOT LIMITED TO THE MANIPULATIONS OF THE RECITED STEPS, ONLY THE STRUCTURE IMPLIED BY THE STEPS

"[E]ven though product-by-process claims are limited by and defined by the process, determination of patentability is based on the product itself. The patentability of a product does not depend on its method of production. If the product in the product-by-process claim is the same as or obvious from a product of the prior art, the claim is unpatentable even though the prior product was made by a different process." *In re Thorpe*, 777 F.2d 695, 698, 227 USPQ 964, 966 (Fed. Cir. 1985) (citations omitted) (Claim was directed to a novolac color developer. The process of making the developer was allowed. The difference between the inventive process and the prior art was the addition of metal oxide and carboxylic acid as separate ingredients instead of adding the more expensive pre-reacted metal carboxylate. The product-by-process claim was rejected because the end product, in both the prior art and the allowed process, ends up containing metal carboxylate. The fact that the metal carboxylate is not directly added, but is instead produced in-situ does not change the end product.).

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

A person shall be entitled to a patent unless –

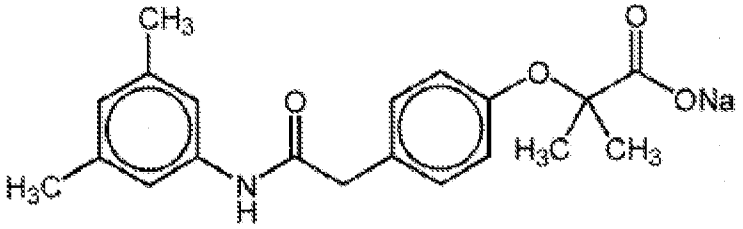
(a) the invention was known or used by others in this country, or patented or described in a printed publication in this or a foreign country, before the invention thereof by the applicant for a patent.

Claims 1-6, 38-41, and 55-66 are rejected under 35 U.S.C. 102(a) as being anticipated clearly by Johnson et al (WO 03/086324). .

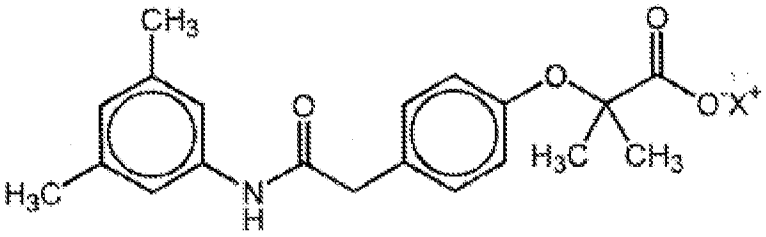
Johnson et al discloses the followings(see abstract):

(57) Abstract: A pharmaceutical composition of 2-[4-[2-[(3,5-dimethylphenyl)amino]-2-oxoethyl]phenoxy]-2-methyl-propionic acid or its physiologically acceptable salts suitable for parenteral administration includes an aqueous formulation of 2-[4-[2-[(3,5-dimethylphenyl)amino]-2-oxoethyl]phenoxy]-2-methyl-propionic acid or its physiologically acceptable salt and a buffer to maintain the pH from about 6 to about 11. The composition in accordance with the invention reduces the amount of particulate matter that forms in solution after heat sterilization. The invention also includes a process for making a pharmaceutical composition of 2-[4-[2-[(3,5-dimethylphenyl)amino]-2-oxoethyl]phenoxy]-2-methyl-propionic acid or its physiologically acceptable salt that has a shelf life in excess of thirty days and is useful in parental administration.

The sodium salt of 2-[4-[2-[(3,5-dimethylphenyl)amino]-2-oxoethyl]phenoxy]-2-methyl-propionic acid ($C_{20}H_{22}NO_4Na$; Molecular Weight = 363.38) has the following structure:



These compounds may be used in the composition in its acid form or in the form of a physiologically acceptable salt. The physiologically acceptable salt of 2-[4-[2-[(3,5-dimethylphenyl)amino]-2-oxoethyl]phenoxy]-2-methyl-propionic acid can be represented as having the following general structure where X^+ represents the cation of the physiologically acceptable salt:



The salt may include compounds with inorganic or organic cationic counterions. For example, inorganic counterions may include, but are not limited to, sodium, potassium, calcium, magnesium, zinc, and combinations thereof. Organic counterions may include, but are not limited to, lysine, hydroxy-lysine, histidine, arginine, ornithine, tromethamine, meglumine, and combinations thereof.

> The allosteric modifying compound is preferably placed in solution prior to administration. The solution may be made using water, a saline solution, a dextrose solution, a lactated Ringer's solution, an aqueous solution of mannitol, or combinations thereof as the diluent. Other diluents may be used as long as they are suitable for parenteral administration to a patient. Preferably, the diluent does not reduce the chemical or physical (particle) stability of the allosteric modifying compound such that it fails the (USP) 25 <788>requirement.

(see page 17 ,lines 1-22). This is identical with the claims.

Because the prior art expressly can teach the same compound in a variety of crystalline forms just as the instant claims, the measurements of FTIR spectrum, and X-ray powder diffraction pattern recited in the claims would be inherent features in the absence of evidence to the contrary.

Applicants are advised that ***In re Best*** , 562 F.2d 1252, 195 USPQ 430 (CCPA 1977) states: where, as here, the claimed and prior art product is identical or substantially identical , or produced by an identical or substantially identical process, the PTO can request an applicant to prove that the prior art product does not necessarily possess the characteristics of the claimed product---- whether the rejection is based on " inherency " under 35 USC 102 , on " prima facie obviousness " under 35 USC, jointly or alternatively, the burden of proof is the same , and its fairness is evidenced by the PTO's inability to manufacture products or to obtain and compare prior art products." Note ,also, " products which are merely different forms of known compounds, notwithstanding that some desirable results are obtained therefrom, are unpatentable where products have same utility as the art compounds; the invention can be present if the prior art product can not be used for the purpose asserted for pure or

new form of product; merely changing form, purity, color or other characteristics of old product with a new use as a result thereof does not render product patentable where utility remains the same ; stability of product does not confer patentability thereon even though a new result is asserted; moreover, advantages in use of product can not be considered of patentable significance. ***Ex parte Hartop***(139 USPQ 525).

Limitations from the specification cannot be read into claims and the examiner has used the claims as presented. There is no distinguishing feature in the claims that prevents the claims from reading on the prior art crystalline form. As such , the prior art anticipates clearly the instant claims.

Claim Rejections - 35 USC § 103

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the

invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

The factual inquiries set forth in *Graham* **v.** *John Deere Co.*, 383 U.S. 1, 148 USPQ 459 (1966), that are applied for establishing a background for determining obviousness under 35 U.S.C. 103(a) are summarized as follows:

1. Determining the scope and contents of the prior art.
2. Ascertaining the differences between the prior art and the claims at issue.
3. Resolving the level of ordinary skill in the pertinent art.
4. Considering objective evidence present in the application indicating obviousness or nonobviousness.

Claims 1-41,52,54-59, and 60-66 are rejected under 35 U.S.C. 103(a) as being unpatentable over Johnson et al (WO 03/086324) in view of Byrn et al (Solid-State chemistry of Drugs, 2nd. ed. 1999, p. 233-236).

Johnson et al discloses the followings(see abstract):

(57) **Abstract:** A pharmaceutical composition of 2-{4-{2-{(3,5-dimethylphenyl)amino}-2-oxoethyl}phenoxy}-2-methyl-propionic acid or its physiologically acceptable salts suitable for parenteral administration includes an aqueous formulation of 2-{4-{2-{(3,5-dimethylphenyl)amino}-2-oxoethyl}phenoxy}-2-methyl-propionic acid or its physiologically acceptable salt and a buffer to maintain the pH from about 6 to about 11. The composition in accordance with the invention reduces the amount of particulate matter that forms in solution after heat sterilization. The invention also includes a process for making a pharmaceutical composition of 2-{4-[2-{(3,5-dimethylphenyl)amino]-2-oxoethyl}phenoxy}-2-methyl-propionic acid or its physiologically acceptable salt that has a shelf life in excess of thirty days and is useful in parental administration.

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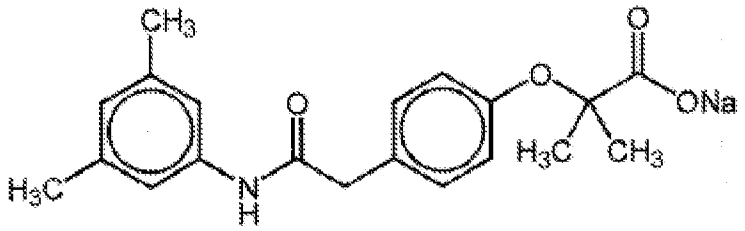
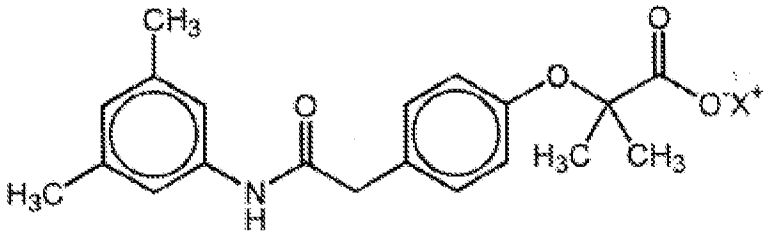


These compounds may be used in the composition in its acid form or in the form of a physiologically acceptable salt. The physiologically acceptable salt of 2-{4-[2-[(3,5-dimethylphenyl)amino]-2-oxoethyl]phenoxy}-2-methyl-propionic acid can be represented as having the following general structure where X^+ represents the cation of the physiologically acceptable salt:



The salt may include compounds with inorganic or organic cationic counterions. For example, inorganic counterions may include, but are not limited to, sodium, potassium, calcium, magnesium, zinc, and combinations thereof. Organic counterions may include, but are not limited to, lysine, hydroxy-lysine, histidine, arginine, ornithine, tromethamine, meglumine, and combinations thereof.

The allosteric modifying compound is preferably placed in solution prior to administration. The solution may be made using water, a saline solution, a dextrose solution, a lactated Ringer's solution, an aqueous solution of mannitol, or combinations thereof as the diluent. Other diluents may be used as long as they are suitable for parenteral administration to a patient. Preferably, the diluent does not reduce the chemical or physical (particle) stability of the allosteric modifying compound such that it fails the (USP) 25 <788>requirement.

(see page 17 ,lines 1-22).

However, the instant invention differs from the prior art in that the solvate form of efaproxiral sodium in water, ethanol, methanol and acetone is unspecified; four or seven moles of water per mole of efaproxiral sodium is also unspecified.

Byrn et al teaches the followings (see page 234, third paragraph) :

Another aspect of solvate formation is that virtually any laboratory solvent can be involved; Table 11.3 lists solvents in solvates reported in the crystal structure literature on organic compounds which, naturally, includes many crystalline drugs. In some solvates, two or even three different solvents occupy their own positions in the structure. Furthermore, a compound may form solvates with a given solvent in different ratios, 2:1, 1:1, etc., and in rare cases, a fixed ratio in polymorphic forms.

Table 11.3 Solvents that Form Solvates with Drugs and Organic Compounds

water
methanol, ethanol, 1-propanol, isopropanol, 1-butanol, *sec*-butanol, isobutanol, *tert*-butanol
acetone, methyl ethyl ketone
acetonitrile
diethyl ether, tetrahydrofuran, dioxane

(see page 236, table 11.3).

Johnson et al expressly teaches that the efaproxiral compound can be in the form of sodium as well as inorganic or organic cationic counterions or combinations; furthermore, Byrn et al advocates that most drugs can form solvates with a given solvent in a different ratio. In addition, Byrn et al addresses the formation of solvates of

many drugs with the following good motivations (see page 236, a middle paragraph) :

- They are often the penultimate solid form of the drug (which should therefore be monitored carefully in the interests of good control).
- They are often specifically chosen for recovery or purification.
- They may have a morphology conducive to good filtration or other bulk processes.
- They may be the only crystalline form available for X-ray structure determination of a new molecular species.
- They may be useful in their desolvated form as a drug product due to superior dissolution properties.
- They may be patentable for any of the above reasons, thus prolonging the manufacturing exclusivity of the drug.

Therefore, if the skilled artisan in the art had desired to form the solvates of well-known efaproxiral sodium, it would have been obvious to the skilled artisan in the art to be motivated to employ the teachings of Byrn et al in the Johnson et al process. This is because Byrn et al does provide good incentives to develop the solvates of well-known efaproxiral sodium; the skilled artisan in the art would expect such a manipulation to be successful and feasible as guidance shown in the prior art.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Taylor Victor Oh whose telephone number is 571-272-0689. The examiner can normally be reached on 8:30-5:00.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Janet Andres can be reached on 571-272-0867. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

Taylor Victor Oh, MSD,LAC
Primary Examiner
Art Unit :1625

/Taylor Victor Oh/
Primary Examiner, Art Unit 1625
5/20/10